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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P035667WO:CJM		FOR FURTHER ACTION	See Form PCT/PEA/416
International application No. PCT/GB2004/004390	International filing date (day/month/year) 15.10.2004	Priority date (day/month/year) 15.10.2003	
International Patent Classification (IPC) or national classification and IPC B01J19/00, H01L51/30			
Applicant OXFORD GENE TECHNOLOGY IP LIMITED			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> sent to the applicant and to the International Bureau) a total of 3 sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>			
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand 13.06.2005		Date of completion of this report 31.01.2006	
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016		Authorized Officer Veefkind, V Telephone No. +31 70 340-1017 	

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/004390

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

Description, Pages

1-23 as originally filed

Claims, Numbers

1-10 as originally filed

11-41 filed with telefax on 30.01.2006

Drawings, Sheets

1/5-5/5 as originally filed

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/GB2004/004390

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-41
	No: Claims	
Inventive step (IS)	Yes: Claims	1-41
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-41
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Reference is made to the following documents:

- D1: WO 03/020415 A2 (ISIS INNOVATION LIMITED; SOUTHERN, EDWIN, MELLOR; EGELAND, RYAN, D) 13 March 2003 (2003-03-13)
- D2: US-B1-6 630 359 (CAILLAT PATRICE ET AL) 7 October 2003 (2003-10-07)
- D3: US-A-6 093 302 (MONTGOMERY ET AL) 25 July 2000 (2000-07-25)
- D4: WO 01/43870 A (MOTOROLA INC; SHI, SONG; ZHANG, PEIMING; MARACAS, GEORGE; MARACAS, GEO) 21 June 2001 (2001-06-21)
- D5: WO 98/01758 A (NANOGEN, INC) 15 January 1998 (1998-01-15)

Re Item V

Subject to the remark about independent claim 13 (which is unclear) in Item VIII, the following is observed.

1. Document D1 discloses a method and a device for electrochemically treating a substrate with electrodes producing first and second quenchable redox products. The electrodes are individually addressable (see step (b) in claim 20) and there can be one common counter electrode (see claim 25). The subject-matter of independent claims 1 and 13 differs from D1 in having a common first electrode arranged to define cells therein.

Document D2 (see passages cited in the Search Report) describes a system and method for electrochemically treating a substrate. It has an arrangement of a common first electrode (9b) or (29) in Figures 1 and 2) arranged to define cells therein and individually addressable second electrodes. In column 1, lines 26-38, it becomes clear that this document is concerned with the demand for systems enabling the chemical or biological analysis with a very large number of points (i.e., high resolution). D2, however changes the surface of the addressable electrodes itself and not of a substrate above it. The subject-matter of claims 1 and 13 differs in that the electrodes and the substrate are separated by the electrolyte. It is not suitable for patterning several substrates

Document D3 discloses a method and a device for electrochemically treating a substrate with addressable electrodes and "getter" electrodes arranged to define cells around the addressable electrodes (see for example Figure 36). The electrolyte (usually

water) is such that the second redox product (H^+) is quenchable by the first redox product (OH^-). The "getter" electrode may be used in conjunction with a scavenging solution and has the function of scavenging electrochemically generated reagents that may diffuse away from the electrode. The subject-matter of claim 1 differs from D3 in that the substrate appears to be separated from the device (the device faces the substrate), the first electrode is "common", and that the getter electrodes appears to be not necessarily the counter electrodes.

The subject-matter of independent claims 1 and 13 is therefore novel (Article 33(2) PCT).

Document D1 is at present considered to be the closest prior art.

The difference with D1 seems to be twofold: the electrode is "common" and it defines cells. This seems to lead to a simple arrangement allowing modification of a substrate with improved resolution.

The problem to be solved appears to be the provision of a means for repeatedly patterning different substrates (excluding D2 and D3 which deal with electrodes on a substrate as closest prior art) comprising a simple arrangement allowing improved resolution.

It is not straightforward to at the same time provide improved resolution and a simple device. The arrangement of claims 1 and 13 surprisingly achieves this goal.

The subject-matter of claims thus 1 and 13 appears to involve an inventive step (Article 33(3) PCT).

The dependent claims as such then also meet the requirements of the PCT with respect to novelty and inventive step.

Although the category and dependency of claims 31-38 is unclear, they would also be novel and inventive if they would properly depend on claim 1.

Independent claims 39 and 41, as well as dependent claim 40, appear to be novel and

inventive for the same reasons as mentioned for claim 1.

Re item VIII

1. Independent claim 13 is unclear (Art. 6 PCT). It defines the device, *inter alia*, by means of the electrolyte which is in contact with the substrate during use. This throws doubt upon the category of the claim (use-claim or entity claim?) and (therefore) the scope of desired protection.

If "during use" had not been in the claim, it would have been acceptable under Art. 6 PCT. Basis for the omission of "during use" appears to be present on page 2, lines 23-25.

2. Claims 21,29-41 do not comply with the requirements of Article 6 PCT.

Claims 21,29 and 30 are formulated in such broad terms, referencing to (parts of) other unspecified devices that the scope of protection could not be clearly determined.

For claims 31-38 both the category and the dependency, and even if they are to be considered as independent or dependent, are not well defined.

The combination of independent claims 1, 39 and 41 leads to a multiplicity of independent claims in the same category. Although these claims have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought and/or in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.

11. The method of any preceding claim, wherein the substrate material is impermeable.
12. The method of any preceding claim, wherein the substrate material is a glass, a plastic, a metal, a semiconductor, a silicon oxide or a gel.
13. A device for electrochemically modifying a substrate, the device having:
- 5 (i) a common first electrode arranged to define cells therein; and
- (ii) a plurality of individually addressable second electrodes,
- wherein:
- (a) a plurality of the cells contain individually addressable second electrodes;
- (b) the common first electrode and the plurality of second electrodes are in contact with an
- 10 electrolyte;
- (c) the electrolyte is in contact with the substrate during use, the substrate being the surface of a material which is separate from and facing the electrodes; and
- (d) the electrolyte is such that the common first electrode is able to generate a first redox product, the second electrode is able to generate a second redox product, and the second
- 15 redox product is quenchable by the first redox product.
14. The device of claim 13, wherein the common first electrode is a cathode and the second electrodes are anodes.
15. The device of any one of claims 13-14, wherein the common first electrode is singly addressable such that the potential of the first electrode may be altered by addressing a single connection.
- 20 16. The device of any one of claims 13-14, wherein the common first electrode is a bus line which is neither switchable nor addressable.
17. The device of any one of claims 13-16, wherein the common first electrode has a geometry in which there is a substantially regular pattern, such as a grid, a net, a honeycomb, a series of intersecting circles or other tessellating shapes.
- 25 18. The device of any one of claims 13-17, wherein the arrangement of the common first electrode results in at least $n \times 10^6$ cells, where n is 0.5 or more.
19. The device of any one of claims 13-18, wherein the arrangement of the common first electrode is such that the distance between the centre of a cell and the centre of at least one of its immediate neighbour cells is less than 0.5 mm.
- 30 20. The device of any one of claims 13-19, wherein the second electrodes are addressed using a direct connection from an electrode to a bond pad on the perimeter of the device, by CMOS switching circuitry, or by transistor-based circuitry.

21. The device of claim 20, wherein the second electrodes are addressed using TFT circuitry.
22. The device of any one of claims 13-21, wherein the distance between the centre of a second electrode and the centre of at least one of its neighbouring second electrodes is less than 0.5 mm.
23. The device of claim any one of claims 13-22, comprising at least $n \times 10^6$ second electrodes, where n is 0.5 or more.
24. The device of any one of claims 13-23, wherein the ratio of the number of cells to the number of second electrodes is less than 1.
25. The device of any one of claims 13-23, wherein the ratio of the number of cells to the number of second electrodes is more than 1.
26. The device of any one of claims 13-23, wherein the ratio of the number of cells to the number of second electrodes is substantially 1.
27. The device of claim any one of claims 13-26, wherein the common first electrode and second electrodes are made from materials independently selected from indium tin oxide, iridium, platinum, palladium, gold, silver, copper, nickel, zinc, titanium, tungsten, aluminium and alloys of these metals.
28. The device of claim 27, wherein the common first electrode and second electrodes comprise a coating of iridium on another material.
29. The device of any one of claims 13-28, wherein the support on which the second electrodes are positioned and the circuitry connecting the second electrodes are as found in liquid crystal display devices.
30. The device of any one of claims 13-29, wherein incorporated into a flow cell arrangement.
31. The method of any one of claims 1 to 12, or the device of any one of claims 13 to 30, for use in deprotecting a substrate in specific patterns.
32. The method or device of claim 31, for use in removing protecting groups from specific regions of a substrate to leave a pattern of deprotected groups, such that subsequent exposure of the deprotected groups to a reactant allows the deprotected groups to react with the reactant.
33. The method or device of claim 31, for use in combinatorial synthesis.
34. The method or device of claim 31, for use in the synthesis of libraries of small organic compounds bound to a surface.
35. The method or device of claim 31, for use in synthesising polymers.

36. The method or device of claim 34, for use in synthesising polynucleotides, polysaccharides, or polypeptides.
37. The method or device of claim 31, for etching of the substrate.
38. The method or device of claim 31, for use in the production of organic LED materials.
- 5 39. A method for preparing an array of polynucleotides comprises the steps of:
- (1) providing a substrate having protecting groups on its surface and which faces the device of any one of claims 13 to 30 and is in contact with the electrolyte;
 - (2) switching a first set of second electrodes so as to generate a second redox product which exposes deprotected groups by removing a set of protecting groups from the substrate;
 - 10 (3) coupling a nucleotide to the set of deprotected groups, the nucleotide comprising a protecting group; and
 - (4) repeating the sequence of steps (2) and (3) until the desired array has been generated.
40. The method of claim 39, wherein the second redox product is a proton and the protecting group is an acid-labile protecting group which protects a furanyl hydroxyl group.
- 15 41. A method for guiding a reagent along the face of a substrate in a desired path, wherein a device of any one of claims 13 to 30 is used to create redox products along the desired path, and wherein the reagent moves into region(s) where the redox products are created.

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